

**REMARKS**

The claims have been amended to more clearly describe the current invention and no new matter has been introduced. Claim 36 has been added, but claim 18 has been cancelled, so the total number of pending claims remains the same.

**1. Rejections Under 35 USC § 112 (first paragraph)**

The Examiner has rejected claims 1-35 under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. This rejection is traversed.

The Examiner states that the terms, "an anchoring domain," in claim 1 and, "said additional domain," in claim 6 are vague and confusing. Applicants have amended claims 1 and 6 to better clarify the identity of each domain, placing them in proper form and obviating the rejection.

The Examiner states that claim 30 should recite the SEQ ID No, rather than refer to figure 6.10. The applicants have amended the claim 30 to recite SEQ ID No. 75, thereby obviating the rejection.

**2. Rejections Under 35 USC § 103**

The Examiner has rejected claims 1-8, 10-11, 19-21 under 35 USC § 103 as being unpatentable over Holliger et al. in view of Barbas et al. The Examiner states that Holliger et al. teach a composition that comprises two domains, a binding domain positioned C-terminal to a second domain, and the two domains are expressed in a biological display system to identify a predetermined epitope of interest.

The Examiner states that Barbas et al. teach using the C-terminal domain of the gene III protein in a phage display library assay to mediate anchoring and increase sensitivity. The Examiner concludes that it would have been obvious as to incorporate the C-terminal domain of gene III in the phage display system taught by Barbas et al. into the Holliger et al phage display for identifying binding antigen.

The method of the present invention is directed to displaying a panel of "bivalent or multivalent" recombinant polypeptides. Applicants do not agree with the Examiner's combination of references. But even if combined, Applicants submit that even the combined teachings of Holliger et al. and Barbas et al. as suggested by the Examiner do not amount to Applicants' invention. Holliger et al. teaches the VH and VL regions that make up an epitope binding domain in a single polypeptide, spaced by a linker of a few amino acids. Unlike Applicants, Holliger et al. does not teach a protein having either an N-terminal blocking domain or a C-terminal anchoring domain.

Applicants point out that figures 9F and 9G of Holliger et al. depict DNA vectors that drive the expression a single RNA which carries two VH-VL coding sequences in tandem array. However, there are stop codons in the N2 linker that separate the two VH-VL coding sequences. In addition, the N2 linker has a ribosome binding site that facilitates the expression of the VHB-VLA polypeptide. Therefore, there are two polypeptides expressed from the DNA constructs presented in figures 9F and 9G, each of which has only a single VH-VL epitope binding domain. Neither of those polypeptides have an N-terminal blocking domain or a C-terminal anchoring domain.

Barbas et al. teaches a phage display system made of two proteins, an antibody heavy chain fragment fused to a fragment of the GenIII protein from filamentous phage and an antibody light chain fragment. The nucleotide sequences that encode these proteins and drive their expression are carried in a single vector, but the VH-GenIII fusion and the VL proteins are completely independent as their expression is directed by different RNAs (Figure 1, Pg. 7979). Neither of the proteins taught by Barbas et al. contain an N-terminal blocking domain or a VH and VL domain in a single protein.

It follows that the combination of Holliger et al. and Barbas et al. amounts to a protein made up of a VH, VL, and a Gene III protein fragment. Consequently, the combined Holliger et al. / Barbas et al. protein lacks the N-terminal blocking domain of the Applicants' invention.

Accordingly, the Examiner's prior art rejection should be withdrawn.

**3. Patentably Distinct Invention**

The Examiner has misconstrued and misrepresented the Applicants' arguments concerning proper examination procedure following a finding that an elected species is allowable. The Examiner states that the Applicants argued that elected SEQ ID No. 75 is not a patentably distinct invention with respect to SEQ ID Nos. 61, 63, 65, 67, 69, 71, 73, and 77 (Pg. 4 of the July 8, 2005 Office Action). The Applicants never made such an argument.

The relevant events and arguments are as follows. In the Office Action dated November 4, 2002, the Examiner imposed restriction and election of species requirements. Applicants traversed these requirements, and, in the Office action dated March 3, 2003, the Examiner found Applicant's arguments against restriction persuasive but maintained the election of species requirement. In the response, Applicants' provisionally elected SEQ ID No. 75, and reserved the right to have additional species examined after the elected species was found allowable (Response to Restriction Requirement July 24, 2004, Pg. 7).

In the subsequent Office Action, dated October 25, 2004, the Examiner stated that SEQ ID Nos. 60-74 are patentably distinct from each other, and that each is considered a patentably distinct invention (Pg. 6). In response, the Applicants pointed out that the Examiner was suggesting that any allowable claims must be limited to SEQ ID No. 75. Applicants submitted that this amounts to an improper restriction of claims, without statutory or regulatory basis (Reply April 25, 2005, Pg. 12).

Finally, the Applicants noted that the Examiner indicated the species of SEQ ID No. 75 is allowable (October 25, 2004 Office action, Pg. 6). The Applicants quoted MPEP §803.2, which states that "once the elected species is found allowable over the prior art, the remaining scope of the claim will be examined fully with respect to the elected species in further to the extent necessary to determine patentability." Based on this authority and the Examiner's indication of SEQ ID No. 75's allowability, Applicants submitted that it was incumbent upon the Examiner to expand the search and examination of the claims to encompass more than just the one species (Reply April 25, 2005, Pg. 12).

At no time did the Applicants make the argument that the Examiner ~~assumed to them in the July 8, 2005 Office Action~~ that applicants ~~should be allowed~~ if the Examiner to expand the search and examination of the claims to encompass more species now that the species of SEQ ID. No. 75 has again been indicated allowable (Office Action July 8, 2005, Pg. 6).

#### **4. Finality of the Office Action**

The Examiner has improperly made the current Office Action final. In the Office Action dated October 25, 2004, the Examiner imposed obviousness rejections over Mack et al. in view of Barbas et al. (Pg. 4) and / or Borreback et al. (Pg 5). In the current Office Action, the Examiner changed the §103 primary reference to Holliger. (Office Action July 8, 2005, Pgs. 3-4). Applicants submit that it is improper to make the current Office Action final in light of the new primary reference the Examiner used to make the current obviousness rejections.

#### **5. Improper Prior Art**

The Examiner cites Rudert et al. as prior art against the present application. However, the present application's European foreign priority filing date is November 17, 1997, which is prior to even Rudert et al.'s PCT filing date of August 3, 1998. Therefore, Rudert et al. does not qualify as prior art against the present application.

In view of the above amendments and remarks, Applicants respectfully request reconsideration of the rejections and allowance of the claims.

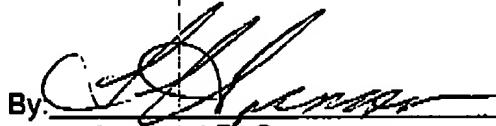
If the Examiner has any questions concerning this application, the Examiner is requested to contact the undersigned at (714) 708-8555 in our Southern California office.

Appl. No.: 09/554,465

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

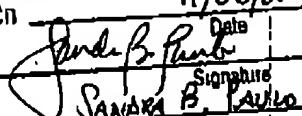
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